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Outcomes of Patients with Respiratory Distress Treated with Bubble CPAP on a Pediatric Ward in Malawi

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ABSTRACT

Objective: To describe the outcomes of infants and young children with respiratory distress when treated with a novel, low-cost, stand-alone bubble Continuous Positive Airway Pressure (bCPAP) system in a resource-limited setting.

Methods: A non-randomized, convenience sample study in a pediatric unit in Blantyre, Malawi, 2013. Patients weighing ≤10 kg with respiratory distress were eligible. We compared outcomes for patients with bronchiolitis, pneumonia and *Pneumocystis jiroveci* pneumonia (PJP) after treatment with bCPAP.

Results: Seventy percent of patients treated with bCPAP survived. Outcomes were best for patients with bronchiolitis and worst for those with PJP. Most survivors (80%) showed improvement within 24 h. All treating physicians found bCPAP useful, leading to a change in practice.

Conclusions: Bubble CPAP was most beneficial to patients with bronchiolitis. Children, who were going to get well, tended to get well quickly. Physicians believed the bCPAP system provided a higher level of care than nasal oxygen.

KEYWORDS: bubble CPAP, respiratory distress, pediatric, resource limited setting, low cost device.

INTRODUCTION

Respiratory failure is a leading cause of morbidity and mortality in children aged <5 years, especially in the developing world [1]. Pneumonia accounts for 20% of all deaths of <5-year-olds worldwide and takes a life every 30 s [2]. More than half of the 6.3 million deaths of <5-year-olds in 2013 could have been prevented by using simple, low-cost interventions [3].

The World Health Organization millennium development goal 4 is to reduce <5-year-olds' mortality by two thirds by 2015. Even to approach this goal, death from respiratory disease must be reduced. To decrease mortality, low-cost, high-functioning

equipment to treat respiratory distress in low-resource settings is required.

Two of the most common methods of providing respiratory support are with mechanical ventilators and Continuous Positive Airway Pressure (CPAP) devices. Owing to high cost and technical complexity, these devices are often not available in resource-limited settings. Commercial ventilators are costly—$45 000–$60 000—and require skilled maintenance, expensive parts and advanced clinical skills to safely intubate and maintain a patient on ventilation [4]. CPAP systems are less expensive and less invasive than ventilators and reduce the risk of barotrauma, infection and other complications. CPAP can be provided conventionally or by bubble CPAP (bCPAP).

In developed countries, bCPAP normally uses wall-piped air and oxygen sources [5]. These are often not available in low-resource settings where hospitals have provided bCPAP by using the flow from an oxygen cylinder that may provide unsafe levels of oxygen.

A team of Rice University bioengineers, Texas Children's Hospital pediatricians and respiratory therapists and University of Malawi College of Medicine pediatricians collaborated to develop a bCPAP system for resource-limited settings. The Pumani (Pumani means breathe in Chichewa) bCPAP system consists of a flow generator that blends room air and oxygen from a cylinder or concentrator. The rest of the system—a flow regulator, pressure generator and patient interface—are similar to those used at hospitals worldwide [5]. The system is inexpensive and easy to repair, maintain, operate and transport. The airflow and pressures delivered are the same as those currently in use at Texas Children's Hospital. Device specifics were published elsewhere [6].

Bubble CPAP is a safe and effective intervention for respiratory distress and is widely used in developed countries [7] but it has not been widely used or studied in low-resource settings or outside the neonatal period. Our goal was to compare the outcomes of infants and young children with respiratory distress owing to different causes treated with the Pumani bCPAP system, in a resource-limited setting. We also evaluated the system's usability to determine whether it could be successfully implemented with available staffing and resources.

PATIENTS AND METHODS

Site and study period

We conducted a non-randomized observational study of outcomes following introduction of bCPAP to treat young children with respiratory distress using convenience sampling from January to July 2013 in a 15-bedded Acute Care Pediatric Unit at Queen Elizabeth Central Hospital (QECH).

The QECH is the largest public government hospital in Malawi and the teaching hospital for the country's only medical school. Twenty-five thousand children are admitted per year. Two thousand—almost 10%—of these admissions are for pneumonia. In an earlier study by Stephen Graham and colleagues at the same hospital, among patients with severe pneumonia for whom a specific cause could be identified, 18% had bacterial pneumonia, with *Streptococcus pneumoniae* being the predominant causative bacteria, and 4.9% had confirmed *Pneumocystis jiroveci* pneumonia (PJP) [8].

The results from a concurrent neonatal study have been reported elsewhere [9].

Children with respiratory distress who fulfilled the inclusion criteria and for whom informed consent was granted were enrolled. Clinical and demographic information, excluding personal identifiers, were recorded.

Inclusion criteria

Patients were eligible if they weighed $\leq$10 kg, had respiratory distress from any cause, were breathing spontaneously and if the treating physician deemed bCPAP appropriate therapy.

Exclusion criteria

Patients were excluded if they weighed $>$10 kg, or had any of the following: a cleft palate, tracheoesophageal fistula, diaphragmatic hernia, severe cardiac instability, severe birth asphyxia, were not considered neurologically viable or were not breathing spontaneously. Patients for whom bCPAP was not deemed appropriate or whose parent or

guardian did not consent received nasal oxygen, the local standard of care.

Study design

This was a non-randomized observational study that compared outcomes for patients with respiratory distress due to bronchiolitis, pneumonia from other causes and PJP. Mortality rate, length of stay, diagnosis and time on bCPAP were recorded. Vital signs and work of breathing were recorded by the patient's nurse or physician at initiation of treatment, 1 h later and then twice daily for the remainder of the hospital stay.

Data collected

Data from children receiving bCPAP treatment during the study period were included in the analysis. Demographic information, diagnosis, weight, HIV status, vital signs, mode and tolerance of feeding, physical examination and method and duration of respiratory support were collected. Records were de-identified.

A modified Respiratory Index of Severity in Children (RISC) score was calculated for each child at enrollment and 24 h after initiating bCPAP therapy (Table 1). The RISC score (developed in South Africa) assigns points to risk factors to predict the probability of death in a young child with a lower respiratory infection [10]. A lower RISC score indicates a better prognosis. As originally defined, the RISC score was calculated for HIV-infected and non-infected children. Because we did not always have this information, we modified the score to include points for HIV exposure or clinical signs of severe HIV disease (Table 1).

Ethical considerations

The study was approved by the College of Medicine Research and Ethics Committee in Malawi (P.05/11/1079) and the institutional review boards at Baylor College of Medicine (H-25857) and Rice University (11-198F). A monitoring committee reviewed data quarterly. Written informed consent was obtained from parents or guardians in the local language.

Applicability

Twelve physicians who cared for patients on bCPAP completed a survey to assess their impressions of its benefit and ease of use.

RESULTS

Seventy-nine children were enrolled in the study and placed on bCPAP between January and July 2013. The mean age was 110 days (range: 8–416 days); 31.6% were HIV exposed and a further 8.9% were HIV infected. Most of the children ($n = 42$, 53%) had bronchiolitis, 21 (26.5%) had pneumonia and 15 (18.9%) had clinical *Pneumocystis jirovecii* pneumonia. One had septicemia.

Table 1. Modified RISC score

Severity of respiratory signs on physical examination		
1. O2 saturation = %	If O2 < 90%	3 points
2. Does the child have moderate or severe recessions? Yes/No	Yes	2 points
3. Has the child been refusing feedings? Yes/No	Yes	1 points
Growth standards		
3. Weight for age z-score = _____	$Z \leq -3$	2 points
	$-2 \leq z < -3$	1 points
	$Z > -2$	0 points
HIV disease		
4. Is the child HIV-infected or exposed? Yes/No	Yes	1 points
5. Does the child have severe HIV disease? Yes/No	Yes	2 points
	Total points: (maximum 11)	

Table 2. Descriptive data for study subjects

Demographic and clinical Data	All CPAP subjects	Bronchiolitis	PJP	Pneumonia
Number of completing study	79	42	15	21
Gender, male, %	46.8%	54.8%	38.1%	40.0%
Age, days (mean, range)	110.1 (8 to 416)	98.6 (22 to 416)	110.1 (8 to 265)	143.5 (8 to 392)
Z-score- weight, (mean, range)	−1.08 (−6.8 to 2.9)	−0.34 (−4.82 to 2.86)*,***	−2.15 (−6.8 to 0.92)***	−1.47 (−6.56 to 1.63)*
% HIV positive	8.9%	0.0%	23.8%	13.3%
% HIV exposed	31.6%	21.4%	66.7%	13.3%
Mean days in hospital (all, survivors)	8.41, 8.15	7.29, 7.62	12.52, 11.13	5.93, 7.71
Mean days on oxygen (all, survivors)	2.80, 2.55	2.21, 2.38	4.74, 3.06	1.90, 2.88
Mean days on CPAP (all, survivors)	3.12, 2.95	2.46, 2.49	5.06, 5.38	2.37, 2.75
Mean days in hospital before starting CPAP (all, survivors)	2.01, 1.80	2.15, 2.22	2.05, 0.69	1.64, 0.71
Initial heart rate (mean, range)	154 (79 to 261)	161 (79 to 261)	163 (120 to 198)	157 (108 to 204)
Initial respiratory rate (mean, range)	69 (32 to 154)	65 (32 to 150)*	67(40 to 106)**	85 (40 to 154)*,**
Initial O2 saturations (mean, range)	87 (40 to 100)	90 (40 to 100)	85 (58 to 100)	80 (46 to 99)
Initial RISC score (average, range)	5.40 (1 to 11)	4.05 (2 to 8)*,***	8.00 (3 to 11)**,***	5.40 (1 to 8)*,**

Number of completing Mean 79; 1 with sepsis.
*,**,***= significant differences, $p < 0.05$.

Table 2 summarizes the clinical findings at enrollment and the duration of treatment stratified by primary diagnosis. Of those with PJP, 66.7% were HIV exposed and 23.8% infected—compared with bronchiolitis and pneumonia cases (21.4% exposed and none infected, 13.3% exposed and 13.3% infected, respectively). HIV positivity was confirmed through polymerase chain reaction testing. Children with PJP were more malnourished, spent longer on bCPAP, on oxygen and in the hospital compared with lower rates in bronchiolitis and pneumonia. The vital signs on enrollment were similar in the three groups.

Figure 1 shows the course of two patients treated with bCPAP. Figure 1A describes a patient with bronchiolitis, who had severe recessions (retractions), hypoxia and tachypnea before initiation of bCPAP. This child improved quickly and ultimately was discharged. Figure 1B shows the course for a patient with PJP. Despite bCPAP, his work of breathing remained severe and his oxygen requirement increased. Twenty-four hours after starting bCPAP, he had shown little to no improvement. Ultimately, the patient died.

Overall, 71% of patients treated with bCPAP survived to discharge (95% CI: 60–81%). Patients diagnosed with bronchiolitis had the best outcomes with a survival rate of 92.9% (95% CI: 85–100%), followed by pneumonia with 53.3% survival (95% CI: 28–79%) and only 38.1% of patients with PJP survived (95% CI: 17–59%) (Fig. 2).

Most diagnoses were made clinically. PJP was diagnosed in patients who were HIV positive or exposed and had marked respiratory distress, essentially clear lungs on examination, and marked hypoxia that was

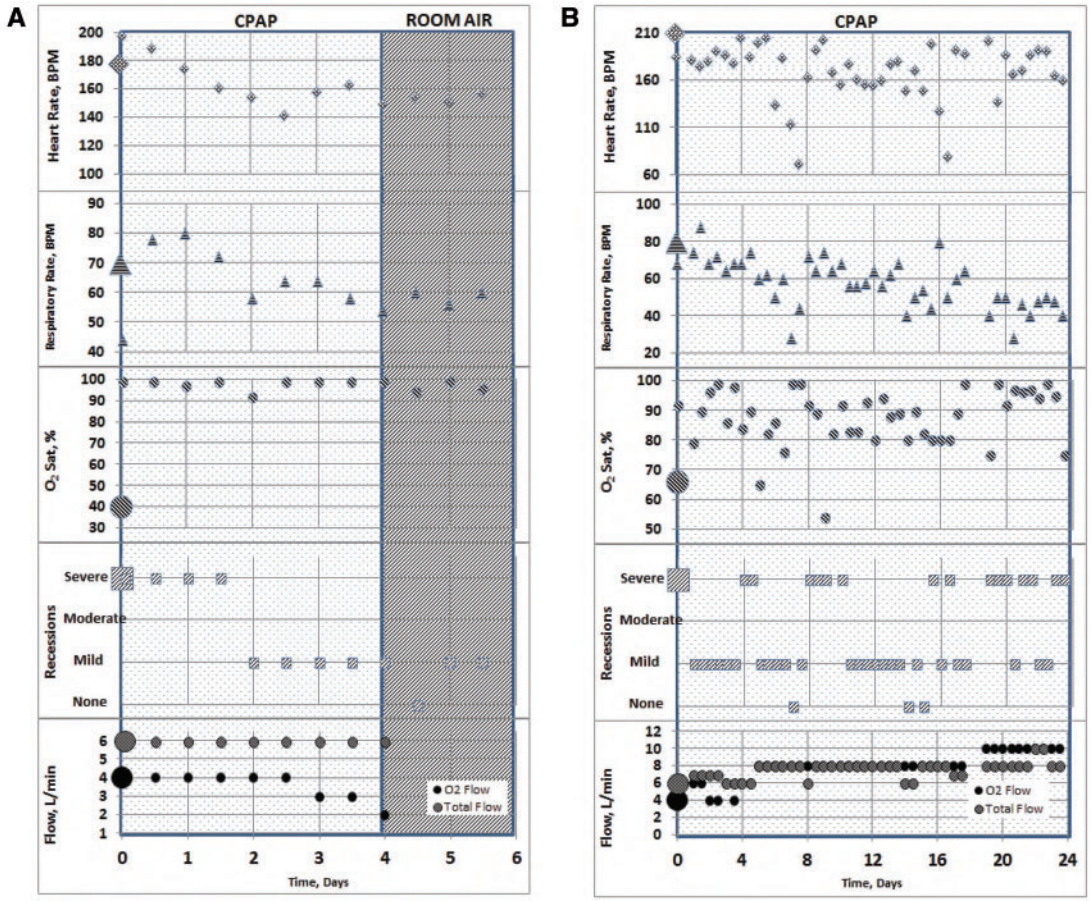

Fig. 1. (**A**) In figure A, the vital signs in white were obtained while the patient was on bCPAP, those in gray were after he was transitioned to room air prior to discharge. (**B**) Vital signs for the course of treatment for a patient with PJP who did not survive.

often unresponsive to oxygen therapy. The discharge diagnosis was used in data analysis. Patients with respiratory illness were routinely treated with antibiotics and some with PJP received steroids. In patients with PJP, tests for cytomegalovirus and ganciclovir treatments were not available.

Figure 3A compares the average modified RISC score at enrollment, stratified by outcome and primary diagnosis. The average modified RISC scores were highest for children with PJP. We calculated the proportion of subjects for whom the RISC score decreased (improved) 24 h after initiating bCPAP therapy (Fig. 3B). Eighty percent of survivors had a lower RISC score after 24 h on bCPAP, indicating that those who did well tended to improve rapidly.

Applicability

All physicians surveyed stated that bCPAP was useful and led to a change in clinical practice. On a scale of 1–5 (5 = highest utility), bCPAP was found most beneficial in bronchiolitis (score = 4.4/5.0) and least beneficial in sepsis (score = 2.7/5.0). Most (11/12) found it easy to decide when to initiate bCPAP. Nine found it easy to decide when CPAP was no longer required. Three found this decision difficult.

DISCUSSION

Patients had a wide range of diagnoses, ages and clinical backgrounds. The treating physicians felt that bCPAP was most helpful in patients with bronchiolitis and least effective for those suffering from PJP.

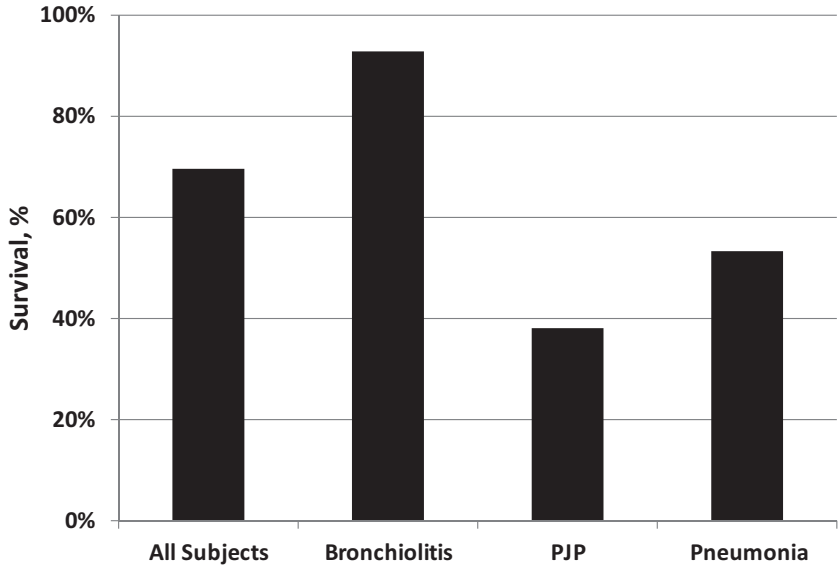

Fig. 2. Percentage of patients treated with bCPAP who survived by primary diagnosis.

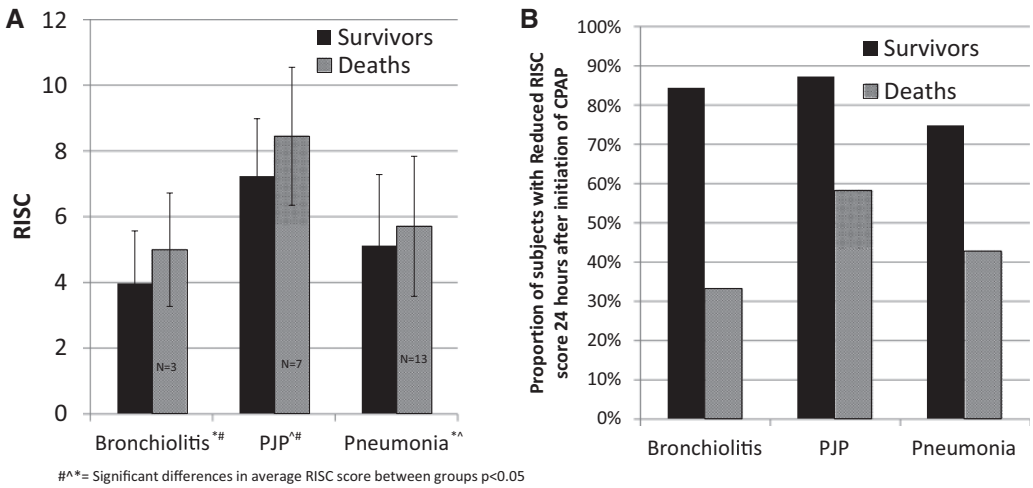

Fig. 3. (**A**) Average modified RISC score at enrollment, stratified by outcome and primary diagnosis. (**B**) Proportion of subjects whose modified RISC score improved 24 h after starting bCPAP treatment, stratified by outcome and primary diagnosis. Error Bars = ±SD.

Note. #^*= significant differences in average RISC score between groups, $p < 0.05$.

This subjective finding corresponds to the results from our study.

The mortality rates in patients with respiratory distress for children not enrolled in the study during this period are unavailable but a study in the same hospital in 2005/2006 found an overall case fatality rate of 10% among children admitted for severe pneumonia, and a 73% case fatality rate for children with PJP pneumonia [8]. The study by Graham was done on a research ward where there are higher nurse to patient ratios and there is greater availability of laboratory and radiological testing, which may explain the lower mortality among their patient population.

The majority of diagnoses in our study were made clinically. While we acknowledge that this may have led to some patients being misclassified, it is standard practice in areas where radiologic and diagnostic tests are not readily available.

To date, there is little high-quality data on the use of CPAP in the treatment of patients with bronchiolitis [11]. Further study is needed to determine its role in the treatment of respiratory distress in infants and young children.

CPAP may not be the first treatment modality chosen for this age-group in settings with other respiratory support options. However, it deserves further study as it poses fewer risks than intubation and mechanical ventilation and is an achievable and potentially useful therapy in resource-limited settings.

FUTURE DIRECTIONS

Clear guidelines on when to initiate and terminate bCPAP therapy would be useful. A larger study is necessary to determine potential benefit to patients with other illnesses such as cardiac failure, gross anemia or sepsis.

Good baseline data that allowed for a comparison of outcomes before and after bCPAP is introduced to a facility, as a potential therapeutic option would strengthen future studies.

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